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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/642,439

Filing Date: August 14, 2003

Appellant(s): BROPHY ET AL.

Frank Rosenberg
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 2/23/2009 appealing from the Office action
mailed 7/22/2008.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,488,838	TONKOVICH et al.	12-2002
2004/0019212	HOVEYDA et al.	1-2004

3,993,855	KANG	11-1976
2002/0182603	CHAPMAN et al.	12-2002
2003/0036474	OSTOJA-STARZEWSKI et al.	2-2003

Haswell et al. "Kumada-Corriu Reactions in a Pressure-Driven Microflow Reactor" Lab on a Chip (2001), pp. 164-166

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1, 3, 5, 7-9, 11, 24, 28, 34-39, 41-42, 47, and 49-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haswell et al., Lab on a Chip, 2001, vol. 1, pp. 164-166 in view of Tonkovich et al. (USP 6,488,838).

Although, Haswell et al. does not teach a microchannel with one wall that is adjacent to a heat transfer microchannel, Haswell et al. does teach using nickel and palladium (column 1, paragraph 1) with a Schiff base ligand that has oxo bridges and is chiral and tethered to a support (scheme1) wherein the support beads are porous (column 4, paragraph 6) and that heat transfer is improved in microreactors, but is silent as to how this heat transfer is achieved. However, because Tonkovich et al. teaches that when using microreactors with microchannels, a conventional way to achieve heat transfer is to arrange a heat transfer microchannel adjacent to a reactor microchannel (column 6, lines 36-38), it would have been *prima facie* obvious to someone of ordinary

skill in the art at the time the invention was made to, modify the teachings of Haswell et al., by incorporating a heat transfer microchannel adjacent to a reactor microchannel to facilitate heat transfer, as suggested by Tonkovich et al.

Although, Haswell is silent as to having a bulk flow because, Tonkovich teaches a bulk flow path, use with microreactors, it would have been *prima facie* obvious to one of ordinary skill in the art to select to use either a bulk flow path or a non-bulk flow path depending on the reaction to be carried out, and the skilled artisan would be expected to be able to select whether or not to use a bulk flow path to optimize the reactor conditions as this would be routine experimentation.

Claims 28, 32, and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haswell et al., *Lab on a Chip*, 2001, vol. 1, pp. 164-166 in view of Tonkovich et al. (USP 6,488,838) as applied to claims 1, 3, 5, 7-9, 11, 24, 28, 34-39, 41-42, 47, and 49-53 above, and further in view of Hoveyda et al. (US 2004/0019212).

Although, Haswell et al. and Tonkovich et al. do not explicitly disclose a dendritic catalyst, they do teach the rest of the limitations of the instant claims. However, because Hoveyda et al. teaches the use of chiral organometallic/transition metal complex that can be in monomeric, polymeric, or dendritic form are stable and recyclable showing superior activity and stereoselectivity, it would have been obvious to someone of ordinary skill in the art at the time the invention was made to combine the teachings of Haswell et al., Tonkovich et al. and Hoveyda et al. with reasonable

expectation of success and the expected benefit of catalyst reactors with high selectivity and stereoselectivity.

Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Haswell et al., Lab on a Chip, 2001, vol. 1, pp. 164-166 in view of Tonkovich et al. (USP 6,488,838) as applied to claims 1, 3, 5, 7-9, 11, 24, 28, 34-39, 41-42, 47, and 49-53 above, and further in view of Kang (US Patent No. 3,993,855).

Although, Haswell et al. and Tonkovich et al. do not explicitly disclose the specific Ni, Rh, or Ir catalyst, they do teach the rest of the limitations of the instant claims. However, because Kang teaches the use of $\text{RhH}(\text{CO}(\text{PPh}_3)_3$ and that it provides selective hydrogenation (column 1, lines 41-45), it would have been obvious to someone of ordinary skill in the art at the time the invention was made to combine the teachings of Kang with that of Haswell et al. and Tonkovich et al. with a reasonable expectation of success and the expected benefit of forming a selective catalyst system.

Claims 43, 45, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haswell et al., Lab on a Chip, 2001, vol. 1, pp. 164-166 in view of Tonkovich et al. (USP 6,488,838) as applied to claims 1, 3, 5, 7-9, 11, 24, 28, 34-39, 41-42, 47, and 49-53 above, and further in view of Chapman, Jr. et al. (US 2002/0182603).

Although, Haswell et al. and Tonkovich et al. do not explicitly disclose the chloro propyl silanes/amines, they do teach the rest of the limitations of the instant claims. However, because Chapman, Jr. et al. teaches the use of chlorpropylsilane and amino

propyl linkers that link a substrate with a support and that such substrate surfaces feature a uniform distribution of attachment functionality (abstract, scheme 1, and paragraph 0039), it would have been obvious to someone of ordinary skill in the art at the time the invention was made to combine the teachings of Chapman, Jr. with that of Haswell et al. and Tonkovich et al. with a reasonable expectation of success and the expected benefit of uniform distribution of catalyst moieties.

Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Haswell et al., *Lab on a Chip*, 2001, vol. 1, pp. 164-166 in view of Tonkovich et al. (USP 6,488,838) as applied to claims 1, 3, 5, 7-9, 11, 24, 28, 34-39, 41-42, 47, and 49-53 above, and further in view of Ostoja-Starzewski et al. (US 2003/0036474).

Although, Haswell et al. and Tonkovich et al. do not explicitly disclose the use of metallocene, they do teach the rest of the limitations of the instant claims. However, because Ostoja-Starzewski et al. teaches the use of tethered (linked) metallocenes and that these catalyst allow the formation of defect free polyethylene to a degree not achieved with conventional catalyst, it would have been obvious to someone of ordinary skill in the art at the time of the invention was made to combine the teachings of Ostoja-Starzewski et al. with that of Haswell et al. and Tonkovich et al. with a reasonable expectation of success and the expected benefit of forming a catalyst that can produce defect free polyethylene.

(10) Response to Argument

I. Claims 1, 3, 5, 7-9, 11, 24, 28, 32, 34-39, 41-42, 47 and 49-53 are not obvious in view of over Haswell et al., Lab on a Chip (2001), 00. 164-166 in view of Tonkovich et al. (U.S. Patent No. 6,488,838)

Applicants argue that “Haswell et al. teach away from a bulk-flow path: “In the constraints of the microreactor, where the beads are packed in the capillary, the reactive solution is driven through the pores under pressure and the number of catalytic site available for reaction is increased”. This is not persuasive because for a reference to teach away there must be some teaching or suggestion that the proposed combination will not work, a mere teaching that there are better methods or that a certain combination is not desired, does not teach away from a combination.

A. It would not have been obvious to modify the Haswell system by replacing the packed bed with a bulk flow channel.

Appellants argue that there is no motivation nor is it obvious to try to modify Haswell’s reactor with a bulk flow path and that to the contrary Haswell et al. teach the importance of using a packed bed in a microchannel : “In the constraints of the microreactor, where the beads are packed in the capillary, the reactive solution is driven through the pores under pressure and the number of catalytic site available for reaction is increased”, and further argue “In view of Haswell’s teaching of a packed bed and the advantages of a packed bed, it would not have been obvious to do the opposite of what is taught and replace the packed bed with a bulk flow path and conduct a reaction over a tethered catalyst in a reactor with a bulk flow path”. This is not persuasive for at least

the following reasons: 1.) The skilled artisan would appreciate that depending on the catalytic reaction to be carried out and the catalyst type used for this reaction type it is the opinion of the examiner that it would have been obvious to one of ordinary skill in the art at the time of invention to modify the teachings of Haswell, since it was well known at the time of invention that there was more than one type of way to operate a microchannel catalyst bed, 2.) Here it is noted that the instant claims under rejection and discussion fail to claim what is the catalyst species present, what are the reagents, what are the conditions or even what is the type of catalytic reaction desired, 3.) Both of the references teach the use of tethered catalyst and applicants have not persuasively argued as to why it would not have been obvious to either tether the catalyst to the reactor or to a bead, as both these methods are well known, depending upon the reaction type desired as articulated in the rejection. Further appellants have failed to show any criticality or unexpected results for the use of a bulk flow path that are fully commensurate with the scope of the claimed invention, 4.) Although there are advantages to using a packed bed as in Haswell there are also advantages to using a bulk flow path, and there are disadvantages to both (i.e. a bulk flow path is less likely to clog, heat transfer out of the catalyst will be more efficient as the surrounding bead will not act as an insulator in the bulk flow path, some catalyst may be better able to be tethered to the wall of the reactor than to a bead, the bulk flow path would also be expected to posses reduced cost, reduced, weight, reduced waste and reduced complications relative to a packed system because of the added factor brought with the addition of a bead and packing a microchannel among other advantages/disadvantages

that would be readily recognizable to one of ordinary skill in the art at the time of the invention to allow for the use of either of these methods depending upon the catalyst used, the reaction type, the reagents, the products, the reaction conditions, flow rate etc).

B. The claimed invention is nonobvious in view of Applicants' Showing of Unexpected results.

Appellants argue that they have shown unexpected results for conducting the Knoevenagel reaction, where the tether catalyst in a microchannel produced superior results compared to the same reaction in a packed microchannel. This is not persuasive because this in no way establishes criticality for or demonstrated unexpected results for the full scope of the claims when given their broadest reasonable interpretation. Further it is noted that page 19 of the instant specification, which appellants point to show the unexpected results clearly state "These results demonstrate the significantly higher yields at much shorter residence times when this type of catalyst is tethered to the walls of a microchannel reactor compared to conventional packed bed or packed microreactors", this teaching is specific for this specific system, and since there are no comparisons done where the amount/concentration of catalyst can be determined (which would significantly affect this result), this statement is not scientifically supported or shown as valid even for the Knoevenagel reaction based on the evidence given, much less for the broad claims, which would include almost any known catalyst, for any known reaction type, with any known reagent, to produce any known or unknown

product. Further it has not been shown that the other reaction conditions are close enough to allow any valid comparison can be made (i.e. temperature, pressure, flow rate, catalyst loading per unit surface area and/or how this could relate to the surface area vs. volume of reaction channels, amount of mixing, reactant concentration, presence or lack of any diluents/solvents, etc.).

Appellants argue that the declaration submitted by Dr. Brophy shows a comparison of catalyst turnover rate (TOR) was an order of magnitude higher than the packed bed configuration and direct attention towards paragraphs 2-5 of the attached declaration. This is not persuasive for at least the following reasons: 1.) The data cited from the reference of Haswell can not be found in the reference of Haswell even after extensive searching, and as such the examiner respectfully request appellants to point to where in the reference this data from Haswell can be found, 2.) The comparisons use different tethers, which will form catalyst with different ligands and as such no direct comparison can be made, 3.) Appellants have offered no persuasive reasoning as to why one would believe that this system would present an advantage to every known catalyst, 4.) Appellants have not shown why this known method would not have been obvious at least to try, as among the references there appears to be only three ways to run this, either batch or flow-through, and the flow through can be either bulk flow or packed beds and since the reference of Haswell clearly shows an advantage over the batch method, that would leave only two possible methods for one of ordinary skill in the art to modify the reaction characteristics by using a flow-method, which both of the cited references are directed towards, 5.) As even repeatedly pointed out by appellants and

stated in the reference of Haswell teaches “the reactive solution is driven through the pores under pressure and the number of catalytic site available for reaction is increased”, this shows that it was known at the time of invention that not all of the catalyst was present on the surface of the beads and available for reaction, and would lead one of skill in the art to recognize that a method that had all of the catalyst on the surface and readily available to react with incoming reagent would have a higher (TOR) per mmol of catalyst used and 6.) It is noted that appellant’s beliefs and opinions are given little weight as evidence in a declaration (see paragraph 7 of the instant declaration).

Appellants argue that “[W]hen the applicants demonstrate substantially improved results,..... and states that the results are unexpected, this should suffice to establish unexpected results in the absence of evidence to the contrary”. This is not persuasive and the evidence to the contrary is that the alleged results presented in the reference of Haswell can not be found, and no comparison of the amount of catalyst present and available for reaction can be obtained based on the disclosure of the references and the evidence presented by appellants, as such no unexpected results can be seen or demonstrated based on what has been submitted.

Appellants argue that a showing of unexpected results should be compared against a single reference and it is improper to compare the showing of unexpected results against a combination of references. While this may be true it is not persuasive at least for the following: 1.) The unexpected results appellants are attempting to demonstrate are related to a method of use, and not towards the apparatus as claimed,

and the reference of Haswell clearly shows a motivation for trying to find a better system for the catalytic reactions and is the reason Haswell compared packed flow through systems with that of batch reactors, while Tonkovich teaches only the use of the bulk flow path, 2.) Appellants have not shown unexpected results over the reference of Tonkovich, 3.) Looking closer at the abstract of Tonkovich and the instant claim 5 they both teach the use of a porous insert to contain the catalyst, and Tonkovich clearly teaches "the improvement according to the present invention is: the catalyst material is on a porous support material having a porosity that resist bulk flow there through and permits molecular diffusion therein. The porous material further has a length, a width and a thickness, the porous material defining at least a portion of one wall of a bulk flow path through which the at least one reactant passes" (see abstract), 4.) Based on the reasoning immediately above it would appear that even if the reactor is packed, when the solution of reagents is driven through this is considered to be a bulk-flow path (see figure 1 and 2 of the reference of Tonkovich) and 5.) It is noted that the amount of activity is expected to be directly related to the amount of active catalyst present and in a form available to react, and while it is understood that at certain dimensions and using a certain particle size bead with a certain loading, that a catalyst tethered to the walls of a reactor would contain more catalyst surface area than that of a packed bed, but as the size of either of these dimensions changes the ratio of surface between the two different type of flow through reactors will change.

Appellants argue that there are 2 ways to show that an invention is not obvious 1.) a teaching away and 2.) new and unexpected results relative to the prior art, and that

in this case there is ample evidence of both a teaching away and a showing of unexpected results. This is not persuasive for the same reasons given above.

II. Claims 28, 32 and 41 are not obvious in view of over Haswell et al., Lab on a Chip (2001), pp. 164-166 in view of Tonkovich et al. (U.S. Patent No. 6,488,838) and further in view of Hoveyda et al. (U.S. Published Application No. 2004/0019212)

A. Claims 28, 32, and 41 are Patentable.

This argue has been fully considered, but is not persuasive for the same reasons given above, and because applicants have failed to articulate any reasoning for the combination being improper.

B. Claim 28 is separately Patentable

Appellants argue that claim 28 requires the use of a chiral auxiliary, and that as they have argued in pages 11-12 in the amendment filed May 30, 2008, Hoveyda does not qualify as prior art because the present application claims benefit of provisional application serial number 60/403,952 which was published on August 15, 2002, and that the invention is clearly supported. This is not persuasive because Hoveyda claims benefit to provisional application number 60/380,640, which has support for the limitation of using a chiral auxiliary (see page 14, last paragraph before the examples of the specification of 60/380,640 and paragraph 0040 of U.S. 2004/0019212), which

precedes the date of the claimed benefit and shows what was known at the time of reaction, as even applicants admit that the use of a chiral auxiliary is well known.

Appellants argue that Hoveyda does not describe a chiral auxiliary. This is not persuasive as Hoveyda does describe the use of a chiral auxiliary.

Appellants argue that the examiner is incorrect in describing a catalyst as a chiral auxiliary. While this may be true, the reference of Hoveyda still clearly describes the use of a chiral auxiliary, and applicants have not persuasively argued as to why the references could not be combined or why it would not be obvious to use a chiral auxiliary depending upon the reagents used the products desired.

III. Claim 40 is not obvious over Haswell et al., Lab on a chip (2001), pp. 164-166 in view of Tonkovich et al. (U.S. Patent No. 6,488,838) and further in view of Kang (U.S. Patent No. 3,993,855)

This argument has been fully considered, but is not persuasive for the same reasons given above.

IV. Claims 43, 45 and 48 are not obvious over Haswell et al., Lab on a chip (2001), pp. 164-166 in view of Tonkovich et al. (U.S. Patent No. 6,488,838) and further in view of Chapman, Jr. (U.S. Published Patent Application No. 2002/0182603)

This argument has been fully considered, but is not persuasive for the same reasons given above.

V. Claim 46 is not obvious over Haswell et al., Lab on a chip (2001), pp. 164-166 in view of Tonkovich et al. (U.S. Patent No. 6,488,838) and further in view of Ostoja-Starzewski et al. (U.S. Published Patent Application No. 2003/0036474)

This argument has been full considered, but is not persuasive for the same reasons given above.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

James Eric McDonough, Junior Examiner, Art Unit 1793

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